REACTION OF 2-BUTENOLIDE AND 4-BROMO-2-BUTENOLIDE WITH 5-ARYL-2-FURALDEHYDES AND THIOLATES

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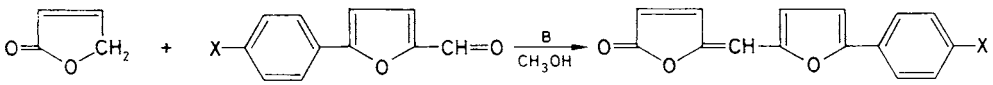
Condensation of 2-butenolide with 5-(4-X-phenyl)-2-furaldehydes (X = H, CH_3, OCH_3, Br, Cl NO_2) in methanol in the presence of piperidine as catalyst afforded the corresponding 4-[5-(4-X--phenyl-2-furfurylidene)]-2-butenolides. As shown by ^{1}H NMR spectra, the reaction afforded mixtures of *Z*- and *E*-isomers which on crystallization were isomerized to the stable *Z*-isomers (except when X = NO_2). 4-Bromo-2-butenolide reacted with sodium salts of 2-mercaptobenzoxazole and 2-mercaptobenzimidazole to give the corresponding 4-(benzazoyl-2-thio)-2-butenolides, probably by an anion-radical mechanism. With arene thiolates, no substitution of the bromo atom took place and the reaction afforded only the corresponding disulfides. The IR and ^{1}H NMR spectra of the synthesized compounds are discussed.

The permanent interest in butenolides and their derivatives is caused by their important biological properties[1,2]. So far, practically no 2-butenolides with heterocyclic residues in position 4 are known, although just such derivatives may have interesting biological properties. Since mastering its industrial preparation[3], 2-butenolide has become available for numerous syntheses and conversions into other heterocycles.

The aim of this study was to find suitable conditions for condensation of aromatic aldehydes with the active methylene group of 2-butenolide, as well as conditions under which the bromo substituent in 4-bromobutenolide can be replaced by a thiolate moiety without opening the lactone ring. 2-Butenolide reacted with aldehydes in methanol at room temperature affording the desired products in high yields only if piperidine was used as catalyst (Scheme 1). Alkali metal hydroxides or alkoxides



I, X = H; *II*, X = CH_3; *III*, X = OCH_3; *IV*, X = Br; *V*, X = Cl; *VI*, X = NO_2

SCHEME 1

were unsuitable because they hydrolysed 2-butenolide. Also other amines were unusable: tertiary amines induced polymerization of 2-butenolide whereas primary amines opened the lactone ring. Because heating the reaction mixture had led to formation of resins, the condensation was carried out at room temperature for 15–48 h. The products separated as crystals and were purified by crystallization from ethanol.

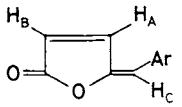
Structure of the compounds was confirmed by elemental analyses (Table I) and IR and ^{1}H NMR spectra (Table II). All the compounds have yellow to orange colour and their UV spectra display two absorption bands at 250–280 nm and 400–440 nm. The IR spectra of compounds *I* – *VI* exhibit pairs of $\tilde{\nu}$(CO) bands at 1 730–1 770 cm^{-1} (for *I*–*III*) and 1 760–1 780 cm^{-1} (for *IV*–*VI*), corresponding to the 2-butenolide carbonyl, conjugated with the exocyclic double bond. The absorption bands at 1 600 to 1 630 cm^{-1} correspond to $\tilde{\nu}$(C=C) vibration and bands at 1 160 cm^{-1} to δ(C—O) vibration of the ester.

TABLE I

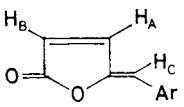
Physical constants and elemental analyses of compounds *I*–*VIII*

Compound R	Formula (mol. wt.)	M. p., °C (yield, %)	Calculated/found			
			% C	% H	% Cl, S,	Br, N
		4-[5-(4-X-Phenyl-2-furfurylidene)]-2-butanolides				
I	$C_{15}H_{10}O_3$	145	75·31	4·23		
H	(238·5)	(80)	75·25	4·21		
II	$C_{16}H_{12}O_3$	147–148	76·17	4·79		
CH_3	(252·3)	(91)	75·89	4·70		
III	$C_{16}H_{12}O_4$	169–170	71·39	4·41		
OCH_3	(268·3)	(23)	71·64	4·48		
IV	$C_{15}H_9BrO_3$	219–220	56·81	2·86	25·20	
Br	(317·1)	(54)	56·53	2·78	25·01	
V	$C_{15}H_9ClO_3$	196–198	66·07	3·33	13·02	
Cl	(272·7)	(75)	65·93	3·24	12·76	
VI	$C_{15}H_9NO_5$	208–210	63·62	3·18	4·86	
NO_2	(283·2)	(60)	63·48	2·95	4·98	
		4-(Benzazolyl-2-thio)-2-butenolides				
VII	$C_{11}H_7NO_3S$	141	56·65	3·02	13·73	6·01
	(233·2)	(65)	56·97	3·82	13·39	5·87
VIII	$C_{11}H_8N_2O_2S$	163	56·89	3·45	13·79	12·07
	(232·3)	(52)	57·21	3·93	12·90	11·44

When monitoring the reaction course by thin-layer chromatography we found that the condensation afforded both geometric isomers (*E* and *Z*):



E – isomer

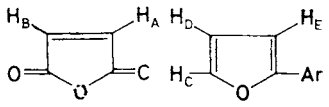


Z – isomer

Purification of the products by crystallization was accompanied by isomerization of *E*-isomers to *Z*-isomers, so that the crystallization afforded pure *Z*-isomers. The only exception was the derivative *VI* which was obtained as a 1 : 2 mixture of *E* and *Z* isomers. The individual isomers of their mixtures are easily identified by chemical shift of the H_C proton of the exocyclic double bond.

TABLE II

^{1}H NMR spectral data for derivatives *I*–*VI*



Compound	H_A	H_B	$J_{H_AH_B}$ (Hz)	H_C	H_D	H_E	$J_{H_DH_C}$ (Hz)	Signals of substitutents
I	7·58	6·19	5·6	6·16	7·18	6·85	3·2	7·1–7 (m, 5H, C_6H_5)
II	7·48	6·18	5·2	6·13	7·17	6·78	3·5	2·39 (s, 3H, CH_3) 7·23 (d, 8·4, 2H) 7·65 (d, 8·4, 2H)
III	7·47	6·17	5·5	6·12	7·14	6·72	3·6	3·85 (s, 3H, OCH_3) 6·95 (d, 8·8, 2H) 7·67 (d, 8·8, 2H)
IV	7·49	6·22	5·5	6·13	7·15	6·84	3·8	7·52–7·65 (m, 4H)
V	7·52	6·27	5·3	6·16	7·21	7·05	3·6	7·86 (d, 8·8, 2H) 8·29 (d, 8·8, 2H)
VI[a]	7·20	6·47	4·5	6·44	6·99	6·73	3·6	7·81 (d, 8·8, 2H) 8·32 (d, 8·8, 2H)
	7·52	6·28	4·5	6·18	7·20	7·05	3·8	7·18 (d, 8·8, 2H) 8·32 (d, 8·8, 2H)

[a] *E*-isomer.

In the spectrum of *Z*-isomers the corresponding signal appears as a singlet at δ 6·1 to 6·2 whereas for the *E*-isomer it is shifted downfield (δ 6·4–6·5) and is split into a doublet ($J_{CB} \sim 0{\cdot}6$ Hz). Moreover, the chemical shifts of the lactone proton signals for both isomers markedly differ (Table II); *e.g.* the H_A proton signals for *E*-isomers are shifted about 0·3 ppm downfield relative to those of *Z*-isomers. The fact that interaction of the lactone vicinal protons is much smaller in the *E*-isomer than in the *Z*-isomer indicates a considerable difference in the lactone ring geometry.

In addition to the synthesis of ylidene derivatives of 2-butenolide, we tried to prepare the hitherto unknown 4-substituted 2-butenolide sulfides by reaction of 4-bromo-2-butenolide with various thiolates.

This reaction gave complex reaction mixtures and we isolated the 4-substituted 2-butanolide sulfides only when using sodium salts of benzazolyl-2-thiols (Scheme 2).

The reaction was carried out at room temperature in acetone in an argon atmosphere. Sulfides *VII* and *VIII* (Table I) are colorless crystalline compounds, insoluble in water, sparingly soluble in ethanol but readily in acetone.

VII, X = O
VIII, X = NH

SCHEME 2

The IR spectra of the compounds *VII* and *VIII* exhibit a doublet at 1 750 and 1 790 cm^{-1} due to unsaturated lactone carbonyl, a $\tilde{\nu}$(C=C) band at 1 600 cm^{-1} and aromatic bands at 1 450 and 1 510 cm^{-1}. The reaction with thiophenol and its derivatives was accompanied by formation of resinous compounds and afforded the corresponding disulfides as the principal products. An ESR spectral study of reaction of 4-bromo-2-butenolide with sodium salt of 2-mercaptobenzimidazole in methanol indicated its anion-radical character. Since thiol radicals, even the sterically hindered ones[4], are very short-lived and recombine to disulfides at room temperature, we proved the formation of sulfide radicals only indirectly by addition of 2,4,6-tri-tert-butylphenoxy radicals, generated from the corresponding trisubstituted phenol. After addition of the reaction mixture devoid of oxygen by introducing argon, the oxygen radicals disappeared immediately as the result of their recombination to compounds containing an —S—O— bond. The formation of disulfides in the reaction with arenethiolates can be explained by recombination of unstable sulfide radicals which, similarly to the carbon radicals of butenolide, can induce polymerization of butenolide leading to resins.

When arenesulfinates were used instead of arenethiolates under the same conditions, no reaction with 4-bromobutenolide occurred. Obviously, the sulfur atom in the sulfinate anion does not afford the electron required for initiation of the anion-radical process.

The formation of the substitution products *VII*, *VIII* with benzazolyl-2-thiolates is apparently enabled by greater stability of the corresponding anions and radicals in which the electron-accepting properties of the heterocyclic moiety may cause a partial delocalization of electrons of the sulphur atoms to the remaining part of the molecule.

EXPERIMENTAL

Infrared spectra of the compounds were recorded on a UR-20 (Zeiss, Jena) spectrometer in Nujol, ^{1}H NMR spectra were measured on a Tesla BS 467 (60 MHz) instrument in deuteriochloroform with tetramethylsilane as internal standard. ESR spectra of the reaction mixture were taken on a Bruker SRC 200D instrument in methanol and acetone.

4-[5-(4-X-*Phenyl*-2-*furfurylidene*)]-2-*butenolides* I—VI

2-Butenolide (0·8; 0·01 mol) and piperidine (0·6 g; 0·007 mol) were added to a saturated solution of 5-aryl-2-furaldehyde (0·01 mol) in methanol. The mixture was stirred at room temperature and the reaction monitored by thin-layer chromatography. The precipitated crystals were collected on filter and crystallized from ethanol.

4-*Bromo*-2-*butenolide*

A mixture of tetrachloromethane (300 ml), 2-butenolide (16·7 g; 0·2 mol), bromosuccinimide (35·6 g; 0·2 mol) and azodiisobutyronitrile (0·1 g) was refluxed for 1·5 h, cooled, and the precipitated succinimide was filtered off. Evaporation of the solvent and distillation at 88°C/8 kPa afforded 20·5 g (63%) of the title compound, n_D^{20} 1·5252, d^{20} 1·9402. The product was a lachrymator and irritated mucous membranes and skin.

4-(*Benzazolyl*-2-*thio*)-2-*butenolides*

Argon was passed through a solution of 4-bromobutenolide (3·26 g; 0·02 mol) in acetone (15 ml) and a solution of sodium salt of benzazolyl-2-thiol (0·02 mol) in acetone was added dropwise. After the end of the reaction, the mixture was poured into water, the crystalline sulfide was filtered and crystallized from ethanol.

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